PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

RUXOLITINIB
POLYCYTHAEMIA VERA (PV)

PROTOCOL REF: MPHARPVPV
(Version No. 1.0)

Approved for use in:

- In the treatment of adult patients with high risk PV that are resistant to or intolerant of hydroxycarbamide

Blueteq registration must be completed prior to treatment initiation

*****PLEASE NOTE THERE IS ALSO A PROTOCOL FOR RUXOLTINIB IN MYELOFIBROSIS AND GRAFT VERSUS HOST DISEASE. PLEASE ENSURE YOU HAVE CHOSEN THE CORRECT PROTOCOL*****

Dosage:

Drug	Dose	Route	Frequency
Ruxolitinib	**10mg**	oral	Twice daily continuously

To continue until progression or unacceptable side effects

Administration:

- If efficacy is considered insufficient and blood counts are adequate, doses may be increased by a maximum of 5 mg twice daily, up to the maximum dose of 25 mg twice daily.
- The starting dose should not be increased within the first four weeks of treatment and thereafter no more frequently than at 2-week intervals
- Ruxolitinib can be taken with or without food

- If a dose is missed, the patient should **not** take an additional dose, but should take the next usual prescribed dose.

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

- Allopurinol 300mg once daily if required for first cycle
- Aciclovir 400mg twice daily

Dosing in renal and hepatic impairment:

Renal		
	Creatinine clearance (mL/min)	**Adjustment**
Ruxolitinib	<30	Recommended starting dose 5 mg twice daily. Monitor closely
	End stage renal disease / haemodialysis	Recommended starting dose is a single dose of 10 mg or two doses of 5 mg given 12 hours apart, to be administered post-dialysis and only on the day of haemodialysis. Monitor closely

Hepatic	
Ruxolitinib	The recommended starting dose is 5 mg twice daily for PV patients with any degree of hepatic impairment Patients diagnosed with hepatic impairment while receiving ruxolitinib should have complete blood counts, including a white blood cell count differential, monitored at least every one to two weeks for the first 6 weeks after initiation of therapy with ruxolitinib and as clinically indicated thereafter once their liver function and blood counts have been stabilised.

Interactions:

Strong CYP3A4 inhibitors

When administering ruxolitinib with strong CYP3A4 inhibitors (such as, but not limited to, boceprevir, clarithromycin, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, saquinavir, telaprevir, telithromycin,

voriconazole) the unit dose of ruxolitinib should be reduced by approximately 50%, to be administered twice daily.

Dual CYP2C9 and CYP3A4 inhibitors

50% dose reduction should be considered when using medicinal products which are dual inhibitors of CYP2C9 and CYP3A4 enzymes (e.g. fluconazole). Avoid the concomitant use of ruxolitinib with fluconazole doses greater than 200 mg daily.

CYP3A4 inducers

Patients should be closely monitored and the dose titrated based on safety and efficacy.

Mild or moderate CYP3A4 inhibitors

No dose adjustment is recommended when ruxolitinib is co-administered with mild or moderate CYP3A4 inhibitors (e.g. erythromycin). However, patients should be closely monitored for cytopenias when initiating therapy with a moderate CYP3A4 inhibitor.

Other medicinal products

Ruxolitinib may inhibit P-glycoprotein and breast cancer resistance protein (BCRP) in the intestine. This may result in increased sytemic exposure of substrates of these transporters, such as dabigatran etexilate, ciclosporin, rosuvastatin and potentially digoxin. Therapeutic drug monitoring (TDM) or clinical monitoring of the affected substance is advised.

It is possible that the potential inhibition of P-gp and BCRP in the intestine can be minimised if the time between administrations is kept apart as long as possible.

For more detailed interactions please refer to the SPC

Main toxicities:

For a full list of reported side effects please refer to the SPC

RUXOLITINIB
Main Toxicities include myelosuppression, infection, bruising, dizziness, headache, constipation, diarrhoea, hypertension, weight gain, hypercholesterolaemia, progressive multifocal leukoencephalopathy, elevated lipase, pneumonia, herpes zoster, urinary tract infection. Please refer to product SPC for a full list of toxicities.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment	X	X	X	X	Prior to every cycle
SACT Assessment (to include PS and toxicities)	X	X	X	X	Every cycle
FBC	X	X	X	X	Prior to every cycle. A cycle may extend to three months in length once patients are stable on treatment. FBC should be taken within 7 days of prescribing but may be taken up to 14 days prior to prescription at clinician's discretion. Prescribers must check FBC prior to prescribing and document that this check has taken place in the medical notes.
U&E & LFTs	X	X	X	X	Must have had within 6 months of prescription. Prescribers must check U+E & LFT prior to prescribing and document that these checks have taken place in the medical notes
CrCl (Cockcroft and Gault)	X	X	X	X	Every cycle
Pregnancy test	X				If clinically indicated
Height and weight	X				Repeat if clinically indicated
Viral Screening (Hep B+ Hep C / HIV / VZZ	X				
Consider skin surveillance	X				As clinically indicated if high risk for skin cancer

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed with cycle if:

ANC ≥ 0.5 x 10^9/L	Haemoglobin ≥120g/L	Platelets ≥ 125 x 10^9/L

Count	Dose modification
ANC < 0.5 x 10^9/L	Suspend ruxolitinib and restart at 5mg BD when ANC has improved to ≥ 0.5 x 10^9/L. Dose can be gradually increased based on FBC
Hb 80 - 120g/L	Consider dose reduction
Hb <80g/L	Suspend ruxolitinib and restart at 5mg BD when Hb has improved to ≥ 80g/L Dose can be gradually increased based on FBC.

	Dose at time of platelet decline				
	25mg BD	20mg BD	15mgBD	10mg BD	5mg BD
Platelet count (x10^9/L)	**New Dose**				
100 - 125	20mg BD	15mg BD	No change	No change	No change
75 - 99	10mg BD	10mg BD	10mg BD	No change	No change
50 - 74	5mg BD	5mg BD	5mg BD	5mg BD	No change
<50	Stop ruxolitinib. Once recovered above these levels, resume ruxolitinib 5mg PO twice a day and gradually increased based on careful monitoring of FBC including white blood cell count differential.				

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

See 'Dosing in Renal and Hepatic Impairment' section.

References:

1. https://www.medicines.org.uk/emc ruxolitinib, Accessed 10/10/23. Updated 24/03/2023
2. NICE: TA921. Ruxolitinib for treating polycythaemia vera. Published date: 18th October 2023

Circulation/Dissemination

Date added into Q-Pulse	16th February 2024
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Version History

Date	Version	Author name and designation	Summary of main changes
Nov 2023	1.0	**Aileen McCaughey – Advanced Pharmacist HO**	New protocol